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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,824	12/15/2005	Christina Gustafsson	026220-00071	8912

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EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
08/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com
IPMatters@arentfox.com
Patent_Mail@arentfox.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,824	GUSTAFSSON ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3 - 26* is/are pending in the application.

4a) Of the above claim(s) *19 - 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3 - 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I in the reply filed on June 12, 2008 is acknowledged. The traversal is on the grounds that the burden to consider all of the groups together is less than the burden on Applicant/the public to prosecute/search the applications/patents separately.

This is not found to be persuasive because a lack of unity has been shown in this National Stage Entry of a PCT and therefore restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claim 19 of the instant application was a use claim and the various interpretations of a use claim resulted in this claim being placed in multiple restriction groups. With the amendment dated June 12, 2008, claim 19 has been amended. It is unclear whether this claim now recites a process for making a composition or a process fro using the composition. Nevertheless, Applicant has elected the composition claims of group I but amended claim 19 is not drawn to a composition. Due to the amendments to the claims, the elected group I now consists of claims 1 – 18.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 3 – 15, 17 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 3, 5 – 11, 13 – 15, 17, 21, 23 and 36 – 38 of copending Application No. 10/507,368 in view of Yuasa et al. (Chem Pharm Bull 1994). The claims of the instant application recite a dosage form comprised of particles of 2-[2-(nitrooxy)ethoxy]ethyl {2-[(2,6-dichlorophenyl)amino]phenyl} acetate ("NO-diclofenac") and either mannitol or lactose.

The claims of '368 recite a solid drug delivery composition comprising a NO-donating NSAID (non-steroidal anti-inflammatory agent), such as NO-diclofenac (see claims 21 and 23).

'368 does not claim the use of porous material comprised of lactose or mannitol.

Yuasa et al. discloses a variety of materials which can be used as porous particles with oily drugs, including calcium silicate, magnesium aluminometasilicate, crystalline cellulose, cornstarch, lactose and dibasic calcium phosphate (figure 1; p 2327, col 1, paragraph 4).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use lactose as the porous particle material, described by Yuasa et al. as a suitable porous particle material, for the solid drug delivery composition of NO-donating NSAIDS as claimed in '368, arriving at the claims of the instant application.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3 – 16, 18 and 19 rejected under 35 U.S.C. 103(a) as being unpatentable over Morein et al. (WO 03/080029) in view of Yuasa et al. (Chem Pharm Bull 1994).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Morein et al. discloses porous particles comprising one or more NO-donating non-steroidal anti-inflammatory (NSAID) compounds, optionally mixed with one or more

surfactants (p 1, ln 5 – 8). Many of these compounds are obtained in an oily form (p 2, ln 1) that make conventional formulation such as tabletting not applicable (p 2, ln 2 – 3). Among the active ingredients disclosed is NO-diclofenac, compound IL on p 8. The porous particles can be composed of calcium silicate, dibasic calcium phosphate, magnesium aluminometasilicate or microcrystalline cellulose (p 10, ln 11 – 15). The porous particles with adsorbed drug are free-flowing powders which can be used to make tablet, capsule or sachet dosage forms (p 10, ln 21 – 27). The particle size of the porous material should be between 50 and 500 μm, particularly between 100 and 150 μm (p 10, ln 29 – 30). The pore size of particles should be between 10 and 1000 Å, particularly 20 and 750 Å (p 11, ln 4 – 5). The particles, capsules and tablets can be coated (p 16, ln 13).

Additionally, a composition comprising a combination of solid particles containing active ingredient and surfactant with particles containing active ingredient and no surfactant are disclosed (p 11, ln 30 – p 12, ln 6). Among the surfactants disclosed as suitable for use in the formulation are non-ionic block copolymers of the poloxamer family (p 12, ln 8 – 17). The ratio of the NO-donating NSAID:surfactant may vary from 1:0.1 to 1:10 (w/w) (p 12, ln 27).

The particles with and without surfactant can be mixed with pharmaceutically acceptable excipients such as fillers, binds, disintegrants, additives, carriers or diluents (p 15, ln 24 – 29).

Morein et al. does not disclose the use or either lactose or mannitol in the particulate material.

Yuasa et al. discloses that calcium silicate, dibasic calcium phosphate, magnesium aluminometasilicate and microcrystalline cellulose and lactose can all be used to make porous dosage forms with oily drugs (see figure 1, p 2328), such as tocopheryl nicotinate (see materials, col 1, p 2327).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare porous materials as taught by Morein et al., and to replace the calcium silicate material with the functionally equivalent lactose, as taught by Yasua et al.

8. Claims 1 and 3 –19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morein et al. (WO 03/080029) and Yuasa et al. (Chem Pharm Bull 1994) as applied to claims 1, 3 – 16, 18 and 19 above, and further in view of Geller et al. (US 5,283,067).

Morein et al. and Yuasa et al. disclose a porous particle dosage form with NO-diclofenac as the active ingredient wherein the porous particle material can be comprised of lactose.

Neither Morein et al. or Yuasa et al. disclose the use of the particles suspended in a water solution.

Geller et al. discloses particle of mannitol, the surfactant PLURONIC®, diclofenac sodium and sodium chloride that are reconstituted with sterilized water (example 4, col 5, ln 50 - col 6, ln 15).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare the particle dosage form as taught by Morein et al. and Yusua et al. and to use those particles as a drug delivery composition in which the active ingredient containing particles are suspended in water, as taught by Geller et al.

Claim 18 recites an intended use of the composition – the treatment of pain or inflammation. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

9. Claims 1, 3 – 7, 9 – 13, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geller et al. (US 5,283,067) in view of Del Soldato et al. (US 5,861,426).

Geller et al. discloses a dry particulate formulation of a salt of diclofenac and optional pharmaceutical acceptable adjuvants (abstract). Among the excipients are surfactants, such as the non-ionic block copolymer surfactants sold using the trade name PLURONIC® (col 2, ln 65 – col 3, ln 32). The ratio of drug to surfactant can range from 1:1.0 x 10^{-4} to 1:0.1, preferable from 1:0.03 to 1:0.1 (col 3, ln 13 – 15). In example 4 (col 5), particles of diclofenac sodium, sodium chloride (a pharmaceutically acceptable excipient), mannitol and PLURONIC® are prepared by lyophilization (col 5, ln 61 – col 6, ln 6). These particles are combined with 1.0 mL of water to prepare a suspension for intramuscular administration (col 6, ln 7 – 15).

Geller et al. does not disclose the use of “NO-diclofenac” in the composition.

Del Soldato et al. discloses anti-inflammatory compounds with terminal $–ONO_2$ groups with improved properties (col 2, ln 1 – 6). Among the compounds disclosed are NO-diclofenac (compound prepared in example 1b, col 18, ln 11 – 28). As shown in table 1 (col 23), NO-diclofenac has improved anti-inflammatory activity with much lower toxicity and only a small decrease in analgesic activity in comparison to diclofenac. Additionally, NO-diclofenac has improved anti-cyclooxgenase and platelet anti-aggregation activity, as shown in table 2 (col 23).

It would have been obvious to one of ordinary skill in the art at the time of the instant application to prepare the formulations of diclofenac as taught by Geller et al. and to use NO-diclofenac as the active ingredient, taught by Del Soldato et al. as having improved therapeutic properties with decreased toxicity. The limitation of “melted form absorbed/adsorbed onto/into” is a product-by-process limitation. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) **MPEP 2113**.

While the final particle size and pore size of the particulates of Geller et al. is not disclosed, there is no evidence that the product does not meet the limitations of these claims. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594)

discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

The ratio of drug:surfactant disclosed by Geller et al. overlaps with that claimed in the instant application. Optimization of this ratio is a results effective parameter. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results.

Claim 18 recites an intended use of the composition – the treatment of pain or inflammation. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

10. Claims 1, 3 – 7 and 9 – 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geller et al. and Del Soldato et al. as applied to claims 1, 3 – 7, 9 – 13, 16 and 18 above, and further in view of Patel et al. (US 6,248,363).

Geller et al. and Del Soldato et al. disclose a particulate dosage form of mannitol, surfactant, and NO-diclofenac. These particles can be suspended in water and administered via injection.

Neither reference discloses the use of the diclofenac particles in a tablet, capsules, or coated tablet/capsule dosage form.

Patel discloses solid pharmaceutical compositions for the improved delivery of active ingredients (abstract), including the active ingredient diclofenac (col 6, ln 59; col 7, ln 1). The compositions can take the form of capsules, tablets, powders or sachets (col 41, ln 38 – 54). The composition and/or the solid particle carriers can be coated with one or more coatings of a variety of types (col 41, ln 55 – 64).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare the NO-diclofenac particles, as taught by Geller et al. and Del Soldato et al. and to select the NO-diclofenac form, given the improved properties, and to formulate those particles into solid dosage forms such as tablets, capsules, coated tablets or coated capsules, taught by Patel et al. as suitable drug delivery dosage forms for these active ingredients.

11. Claims 1, 3 – 13, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geller et al. (US 5,283,067) and Del Soldato et al. (US 5,861,426) as applied to claims 1, 3 – 7, 9 – 13, 16 and 18 above, and further in view of Miller et al. (US 5,763,452) and Nokhodchi et al. (Eur J Pharm Biopharm 2002).

Geller et al. and Del Soldato et al. disclose a particulate dosage form of mannitol, surfactant, and NO-diclofenac.

Neither reference discloses a dosage form comprised of a mixture of particles of NO-diclofenac, some of the particles containing one or more surfactant and some particles without surfactant.

Miller et al. discloses dosage forms of an NSAID and opioid analgesic in which the active ingredients are formulated to provide both immediate and delayed release of the active ingredients (col 3, ln 35 – 49).

Nokhodchi et al. discloses that the inclusion of a surfactant in a matrix alters the release of the active ingredient compared to the matrix without the surfactant (p 349, col 2, paragraph 2, concluding on the next page). The identity of the surfactant, and the concentration of the surfactant are important factors that will regulate the release rate of the drug (p 350, col 1, paragraph 2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare particles of NO-diclofenac as taught by Geller et al. and Del Soldato et al., and to prepare particles both with and without surfactant, as those particles will show different release rates of the drug, as taught by Nokhodchi et al. Such a mixture of release profiles is desirable when administering NSAIDs, as taught by Miller et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW